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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	N/A
Data analysis	N/A

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data that support this study are available within the paper and its Supplementary Information. All primary data underlying the figures reported in the article can be obtained from the corresponding author upon reasonable request.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No statistical methods were used to predetermine the sample sizes. The number of animals in each group was determined according to previous studies cited in our manuscript. The size of each sample is in close agreement with those studies already published and with the need for statistical analysis to discuss the degree of differences and measure the variability of these in vivo data.
Data exclusions	No data were excluded from the analysis.
Replication	All statistical data shown in this paper are based on the paper we published in Science Translation Medicine (Sci Transl Med 12, eaay1063.) All the experimental findings were replicated with the number of replicates, animals and variation shown by n and SD.
Randomization	Therapeutics study: animals were distributed randomly into different groups. Each specific treatment was administrated to animals according to established schedules and regimens.
Blinding	Investigators were blinded when performing therapeutic study. During the experiments designed to evaluate the therapeutic efficiay , animals were randomly divided into control and treatment groups.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Anti-CaMKIIγ (1:400, Novus Biologicals, cat. no. NBP2-15685). https://scicrunch.org/resolver/RRID: AB_2892990. (Novus, Cat# NBP2-15685, RRID:AB_2892990) Anti-Mac2 antibody (1:10, 000, Cedarlane Labs, cat. no. CL8942AP). https://scicrunch.org/resolver/RRID: AB_2814900. (Fluidigm Cat# 3153026B, RRID:AB_2814900) Anti-MerTK (1:500, R&D Systems, cat. no. AF591). https://scicrunch.org/resolver/RRID: AB_2098565. (R and D Systems Cat# AF591, RRID:AB_2098565). Alexa Fluor 647 Goat-anti Mouse IgG (Life Technologies, A-28181). https://scicrunch.org/resolver/RRID: AB_2536165. (Thermo Fisher Scientific Cat# A28181, RRID: AB_2536165).
Validation	Anti-CaMKIIγ (1:400, Novus Biologicals, cat. no. NBP2-15685), Predicted Species: Rat (100%), Porcine (100%), Bovine (100%), Rabbit (100%), Rhesus Macaque (100%), Xenopus (97%). Application: Western Blot 1:500-1:3000, Immunocytochemistry/ Immunofluorescence 1:100-1:1000, Immunohistochemistry, Immunohistochemistry-Paraffin Anti-Mac2 antibody (1:10, 000, Cedarlane Labs, cat. no. CL8942AP), reactivity : human, mouse, rat; Application: immunohistochemistry, immunohistochemistry - paraffin section, immunohistochemistry - frozen section, immunohistochemistry knockout validation. Anti-MerTK (1:500, R&D Systems, cat. no. AF591). Species Reactivity: Mouse. Applicstion: Flow Cytometry 2.5 µg/106 cells, Immunohistochemistry 1-15 µg/mL, CyTOF-ready, Dual RNAscope ISH-IHC.

Alexa Fluor 647 Goat-anti Mouse IgG (Life Technologies, A-28181). Species Reactivity: Mouse. Application: Immunohistochemistry (Frozen) (IHC (F)), Flow Cytometry (Flow), Immunocytochemistry (ICC/IF), Miscellaneous PubMed (Misc)

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HeLa-Luc cells (a HeLa cell line stably transfected with a firefly luciferase reporter gene, Sigma-Aldrich, cat. no. 11033106). https://scicrunch.org/resolver/RRID: CVCL_2939. (ECACC Cat# 11033106, RRID:CVCL_2939) RAW 264.7 (ATCC, TIB-71™). https://scicrunch.org/resolver/RRID: CVCL_0493. (ATCC Cat# TIB-71, RRID:CVCL_0493) HEK-293 (ATCC, CRL-1573™). https://scicrunch.org/resolver/RRID: CVCL_0045. (ATCC Cat# CRL-1573, RRID:CVCL_0045)
Authentication	The cell lines used in the research are regularly checked to ensure they are authentic and are not infected with mycoplasma.
Mycoplasma contamination	All cells were negative for mycoplasma.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell line were used.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Ldlr-/- mice (The Jackson Laboratory, B6.129S7-Ldlrtm1Her/J, Stock No: 002207), Six- to eight-week-old male C57BL/6J mice, 6-week-old female and male BALB/c mice were purchased from the Jackson laboratory (Bar Harbor, ME).
Wild animals	No wild animals were used in this study.
Field-collected samples	This study did not involve samples collected from the fields.
Ethics oversight	All animals received humane care. All procedures were conducted in accordance with protocols approved by the Institutional Animal Care and Use Committees at Harvard Medical School and Columbia University Irving Medical Center.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☐ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Single cell suspensions from cultured cells were used for flow cytometry tests.
Instrument	Flow cytometer (BD LSR Fortessa)
Software	Flowjo v7.6
Cell population abundance	Relevant cell fractions were above 90% for all samples.
Gating strategy	Generally, cells were first gated on FSC/SCC. Singlet cells were usually gated using FSC-H and FSC-A. Debris were removed by thresholding.

☐ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.